Printed: 21-09-2004

NR. 719 0 / 512 4 0 4 0

DT12 Rec'd PCT/PTO 12 JAN 200 EPO - DG 1

CLAIMS

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(68)

1. Use of an estrogenic component selected from the group consisting of: substances represented by the following formula

in which formula R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> independently are a hydrogen atom, a hydroxyl group or an alkoxy group with 1-5 carbon atoms;

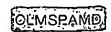
precursors capable of liberating a substance according to the aforementioned formula when used in the present method, which precursors are derivatives of the present estrogen substances, wherein the hydrogen atom of at least one of the hydroxyl groups has been substituted by an acyl radical of a hydrocarbon carboxylic, sulfonic acid or sulfamic acid of 1-25 carbon atoms; tetrahydrofuranyl: tetrahydropyranyl; or a straight or branched chain givcosydic residue containing 1-20 glycosidic units per residue; and mixtures of one or more of the aforementioned substances and/or precursors; in the manufacture of a pharmaceutical composition for use in a method of treating or preventing estrogen-sensitive tumours in a mammal, said estrogen-sensitive tumours being selected from the group consisting of breast cancer and uterine cancer, ovarian cancer, endometriosis, uterine fibroids, benign prostatic hyperplasia and melanoma; and said method comprising the administration of a therapeutically effective amount of the estrogenic component to said mammal and not comprising administration of a GnRH composition.

2. Use of an estrogenic component as defined in claim I in the manufacture of a pharmaceutical composition for use in a method of treating or preventing estrogen-sensitive

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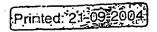
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consisting of breast cancer and uterine cancer, ovarian cancer, endometriosis, uterine fibroids, benign prostatic hyperplasia and melanoma; and said method comprising the administration to said mammal of a therapeutically effective amount of the estrogenic component in combination with an aromatase inhibitor.

- Disc of an estrogenic component as defined in claim 1 in the manufacture of a pharmaceutical composition for use in a prethod of treating estrogen-sensitive tumours in a mammal, said estrogen-sensitive tumours being selected from the group consisting of breast cancer and uteripe cancer, ovarian cancer, endometriosis, uterine fibroids, benign prostatic hyperplasia and melanoma; and said method comprising the administration of a therapeutically effective amount of the estrogenic component to said mammal.
- 2. Use according to <u>any one of claims</u> 1-3, wherein no more than 3 of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> are hydrogen atoms;
  - 3. Use according to any one of claims 1 4 or 2, wherein R<sub>3</sub> represents a hydroxyl group or an alkoxy group.
- 20 4.6. Use according to any one of claims 1-53, wherein at least 3 of the groups R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> represent hydrogen atoms.
  - 5.Use according to any one of claims 1-4, wherein the precursors capable of liberating the estrogenic substance are derivatives of the present estrogen substances, wherein the hydrogen atom of at least one of the hydroxyl groups has been substituted by an acyl radical of a hydrocarbon carboxylic, sulfenic acid or sulfamic acid of 1-25 carbon atoms; tetrahydrofuranyl; tetrahydropyranyl; or a straight or branched chain glycosydic residue containing 1-20 glycosidic units per residue.
- 6.7. Use according to any one of claims 1-65, wherein the method comprises the uninterrupted administration of the estrogenic component during a period of at least 5 days, preferably of at least 30 days.

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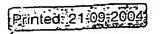






- <u>7.8.</u> Use according to any one of claims 1-76, wherein the method comprises oral, transdermal, intravenous or subcutaneous administration of the estrogenic component.
- 8-9. Use according to claim 87, wherein the method comprises oral administration.
- 9.10. Use according to any one of claims 1-98, wherein the estrogenic component is administered in an amount of at least 1 µg per kg of bodyweight per day, preferably of at least 5 µg per kg of bodyweight per day.
- 10. Use according to any one of claims 1-9, wherein the estrogen sensitive tunours are selected from the group consisting of breast cancer, uterine cancer, ovarian cancer, endometriosis, uterine fibroids, benign prostatic hyperplasia and melanoma.
  - 11. Use according to any one of claims 1-10,0 wherein the estrogen-sensitive tumours are selected from the group consisting of breast cancer and uterine cancer.
    - 12.Use according to any one of claims 1-14, wherein the method comprises on administration of an estrogen suppressant in an amount effective to suppress the endogenous estrogen production, wherein said estrogen suppressant is selected from the group consisting of progestogens, GnRH analogues, aromatase inhibitors, eyelo oxygenase 2 (COX 2) inhibitors, 178 hydroxysteroid dehydrogenase type 1 inhibitors and combinations thereof.
    - 13.12. Use according to claim 211, wherein the aromatase inhibitorestrogen-suppressant is co-administered in an effective amount to suppress blood serum 17β-estradiol level to below 10 pg/ml, more preferably to below 5 pg/ml, most preferably to below 1 pg/ml
    - 14.Use according to claim 11 or 12, wherein the method comprises co-administration of a progestogen
- of an aromatase inhibitor.
  - 16-14. A pharmaceutical composition containing:

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- at least 0.01 mg of an estrogen suppressant selected from the group consisting of aromatase inhibitors. GnRH analogues and combinations thereof;
- b. at least 0.05 mg of an estrogenic component selected from the group consisting of: substances represented by the following formula

in which formula R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> independently are a hydrogen atom, a hydroxyl group or an alkoxy group with 1-5 carbon atoms;

when used in the present method, which precursors are derivatives of the present estrogen substances, wherein the hydrogen atom of at least one of the hydroxyl groups has been substituted by an acyl radical of a hydrocarbon carboxylic, sulfonic acid or sulfamic acid of 1-25 carbon atoms; tetrahydrofuranyl; tetrahydropyranyl; or a straight or branched chain glycosydic residue containing 1-20 glycosidic units per residue; and mixtures of one or more of the aforementioned substances and/or precursors; and

- c. pharmaceutically acceptable excipient.
- 17:15. The pharmaceutical composition according to claim 146, wherein no more than 3 of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> are hydrogen atoms.
- 20 <u>18.16.</u> The pharmaceutical composition according to claim 146 or 157, wherein R<sub>3</sub> represents a hydroxyl group or an alkoxy group.

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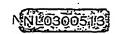
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- 19.17. The pharmaceutical composition according to any one of claims  $1\underline{46}$ - $1\underline{68}$ , wherein at least 3 of the groups  $R_1$ ,  $R_2$ ,  $R_3$  and  $R_4$  represent hydrogen atoms.
- 18. The pharmacoutical composition according to any one of claims 16-19, wherein the precursors capable of liberating the estrogenic substance are derivatives of the present estrogen substances, wherein the hydrogen atom of at least one of the hydroxyl groups has been substituted by an acyl radical of a hydrocarbon carboxylic, sulfonic acid or sulfainic acid of 1-25 carbon atoms; tetrahydrofuranyl; tetrahydropyranyl; or a straight or branched chain glycosydic residue containing 1-20 glycosidic units per residue.
- 21.18. The pharmaceutical composition according to any one of claims 146-1720, wherein the composition contains aromatase inhibitor in an amount equivalent to an oral dosage of at least 0.05 mg anastrozole.
- 22-19. A drug delivery system comprising a pharmaceutical composition according to any one of claims 136-217, said drug delivery system being selected from the group consisting of an oral dosage unit; an injectable fluid; a suppository; a pessary; a gel; and a cream.
- 23.20. A pharmaceutical kit comprising one or more dosage units containing at least 0.05 mg of the estrogenic component as defined in claim 1 and a pharmaceutically acceptable excipient; and one or more dosage units containing at least 0.01 mg of an estrogen suppressant selected from the group consisting of GnRH analogues, aromatase inhibitors, eyelo exygenase 2 (COX 2) inhibitors, 17β hydroxysteroid dehydrogenase type 1 inhibitors and combinations thereof, and a pharmaceutically acceptable excipient.
- 24.21. The pharmaceutical kit according to claim 2023, wherein the dosage units are oral dosage units.